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**Fluorine-19 MRI for detection and quantification of immune cell therapy for cancer.**

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**Public Summary:**

Over the past two decades, immune cell therapy has emerged as a potent treatment for multiple cancers, first through groundbreaking leukemia therapy, and more recently, by tackling solid tumors. Developing successful therapeutic strategies using live cells could benefit from the ability to rapidly determine their in vivo biodistribution and persistence. Assaying cell biodistribution is unconventional compared to traditional small molecule drug pharmacokinetic readouts used in the pharmaceutical pipeline, yet this information is critical towards understanding putative therapeutic outcomes and modes of action. Towards this goal, efforts are underway to visualize and quantify immune cell therapy in vivo using advanced magnetic resonance imaging (MRI) techniques. Cell labeling probes based on perfluorocarbon nanoemulsions, paired with fluorine-19 MRI detection, enables background-free quantification of cell localization and survival. Here, we highlight recent preclinical and clinical uses of perfluorocarbon probes and <sup>19</sup>F MRI for adoptive cell transfer (ACT) studies employing experimental T lymphocytes, NK, PBMC, and dendritic cell therapies. We assess the forward looking potential of this emerging imaging technology to aid discovery and preclinical phases, as well as clinical trials. The limitations and barriers towards widespread adoption of this technology, as well as alternative imaging strategies, are discussed.

**Scientific Abstract:**

Over the past two decades, immune cell therapy has emerged as a potent treatment for multiple cancers, first through groundbreaking leukemia therapy, and more recently, by tackling solid tumors. Developing successful therapeutic strategies using live cells could benefit from the ability to rapidly determine their in vivo biodistribution and persistence. Assaying cell biodistribution is unconventional compared to traditional small molecule drug pharmacokinetic readouts used in the pharmaceutical pipeline, yet this information is critical towards understanding putative therapeutic outcomes and modes of action. Towards this goal, efforts are underway to visualize and quantify immune cell therapy in vivo using advanced magnetic resonance imaging (MRI) techniques. Cell labeling probes based on perfluorocarbon nanoemulsions, paired with fluorine-19 MRI detection, enables background-free quantification of cell localization and survival. Here, we highlight recent preclinical and clinical uses of perfluorocarbon probes and (<sup>19</sup>)F MRI for adoptive cell transfer (ACT) studies employing experimental T lymphocytes, NK, PBMC, and dendritic cell therapies. We assess the forward looking potential of this emerging imaging technology to aid discovery and preclinical phases, as well as clinical trials. The limitations and barriers towards widespread adoption of this technology, as well as alternative imaging strategies, are discussed.

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